original claim 1. New claim 29 finds support in original claim 3. New claim 30 finds support at Specification page 7, lines 11-23 and Table 3, pages 39 and 41.

The claims are amended in response to the Restriction Requirement so as to clarify that they form a single inventive concept in accordance with the requirements of PCT Rule 13.1. A complete copy of all pending claims, including marked up versions of the amended claims is attached hereto.

III. Detailed response to the restriction/election requirement

Applicants wish to thank Examiner Einsmann for her courtesy in extending a telephone interview with the undersigned on December 17, 2002 to discuss in greater detail the pending Restriction Requirement.

The Examiner indicated that if claim 1 were amended to read as a generic or linking claim restricted to one codon region then an election to a species (i.e. one set of probes) would be required for examination purposes.

A. Restriction of claims to codon 82/84

Applicants have amended claim 1 to delete reference to the specific probes of Figure 1 and Table 3. Applicants have also restricted claim 1 to one particular codon region: codon 82/84 (i.e. a target region spanning both codons 82 and 84). Amended independent claims 1, 12, 20 and 26 are now more clearly directed to the generic element of hybridizing at least two probes to a target sequence of the HIV protease gene, codon 82/84.

B. Election of species

Claims 24 and 30 are species claims wherein the two probes of SEQ ID NOs 267 and 354 are elected for initial examination purposes. Both of these probes target codon 82/84. It is

applicants understanding that if the examiner finds claims 24 and 30 patentable, the examiner will broaden the examination to claims directed to the other probes targeting codon 82/84.

C. Claim Relationships

Claims 1, 12, 20 and 26 are generic claims directed to the generic element of hybridizing at least two probes to a target sequence of the HIV protease gene, codon 82/84.

Claims 24 and 30 are the elected species claims directed to the probes of SEQ ID NOs. 267 and 354.

Claims 3 and 23 are subgeneric claims that read on SEQ ID NOs 228-357. These are other probes that target codon 82/84. These claims are generic to and read on the species claims 24 and 30.

Claims 13, 17, 25 and 28 are dependant claims that provide for screening HIV protease codon regions in addition to codon region 82/84.

Claims 16, 19, 21 and 29 are dependant claims that provide a pool of probes useful for the practice of claims 13, 17, 25 and 28.

Applicant asserts that, as recited in MPEP §806.03, the currently pending method kit and solid support claims all define the same essential characteristics of a single embodiment of the invention which provides for an HIV genotyping assay/method (*see* pages 3 and 4 of the specification) of the protease gene, codon 82/84. The recitation of select SEQ ID NOs for representative probes (dependent claims 3 and 23) merely defines the invention in varying breadth or scope; but nonetheless all of the probes listed in claim 3 and 23 share a novel technical feature of the claimed invention. All the probes listed in claim 3 and 23 are capable of simultaneously and specifically hybridizing under the same hybridization and wash conditions to

their respective target sequences of codon 82/84. Further all the probes of claims 3, 16, 19, 21, 23 and 29 share the common features of being 10 to 25 bases in length, have a Tm of between 36°C and 44°C and are capable of hybridizing to their respective target sequences, including codon region 82/84, under stringent hybridization conditions run at 39°C. Consequently, Applicant respectfully requests that restriction of the group I method, kit and composition claims to individual probes be withdrawn as improper, in view of MPEP 806.03.

Further Applicant posits that all the pending claims should be maintained in a single application and not be further divided into separate applications directed to methods and kit/compositions. This application is derived from a PCT application. As such the unity of invention standard set out in the PCT rules dominate. Applicant asserts that claim 1, 12, 20 and 26, which all recite the phrase: "at least two probes specifically hybridizing to a target sequence of the HIV protease gene, codon 82/84 ... wherein said probes are immobilized on a solid support" provides a special technical feature which links the pending claims so as to form a single general inventive concept, thereby fulfilling the requirements for unity of invention under PCT Rule 13.

IV. Conclusion

Applicant believes that the current Response is in full compliance with the requirements set out in the instant Restriction Requirement. In view of the foregoing Amendment and Remarks, Applicant respectfully requests reconsideration and withdrawal of the Restriction Requirement with respect to a single probe in connection with the elected method and kit claims.

In order to facilitate prosecution of this application, Applicants request that the examiner give the undersigned attorney a call at (713) 787-1438 to discuss the restriction requirement before any final determination is made.

Respectfully submitted,

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MARKED-UP VERSION OF CLAIM AMENDMENTS

1. **(Twice Amended)** Method for determining the susceptibility to antiviral drugs of HIV viruses in a biological sample, with said method comprising:

   a) if need be, releasing, isolating or concentrating the polynucleic acids present in the sample;

   b) if need be amplifying the relevant part of a protease gene of HIV with at least one suitable primer pair;

   c) hybridizing the polynucleic acids of step a) or b) with at least two probes specifically hybridizing to a target sequence of the HIV protease gene, ~~said target sequence selected from the group consisting of codon 30; codon 46 and/or 48; codon 50; codon 54; codon 82 and/or 84; codon 90;~~ **codon 82/84,** or the complement of said probe;

   ~~wherein said probes specifically hybridize to any of the target sequences presented in figure 1, or Table 3, or to the complement of said target sequences;~~

   wherein said probes are capable of simultaneously hybridizing to their respective targets under appropriate hybridization and wash conditions;

   wherein said probes are immobilized on a solid support; and

   d) inferring from the result of step c) whether or not a mutation giving rise to drug resistance is present in ~~any of~~ said target sequences.

3. **(Twice Amended)** Method according to claim 1, further characterized in that said probes are chosen from the following list: ~~SEQ ID NO: 7 to SEQ ID NO: 477~~ **SEQ ID NO: 228 to SEQ ID NO: 357**, SEQ ID NO: ~~510~~ **517** to SEQ ID NO: 519 or the complement of said probes.

4. Method according to claim 1 further characterized in that said primer pair is chosen from the following primers: SEQ ID NO: 3, SEQ ID NO: 503, SEQ ID NO: 504, SEQ ID NO: 4, SEQ ID NO: 506, SEQ ID NO: 507, SEQ ID NO: 508 and SEQ ID NO: 509.

5. **(Twice Amended)** Method according to claim 1 further characterized in that:

step b) comprises amplifying a fragment of the protease gene with at least one 5'-primer specifically hybridizing to a target sequence located at nucleotide position 210 to 260 of the protease gene, in combination with at least one suitable 3'-primer~~, and~~

~~step c) comprises hybridizing the polynucleic acids of step a) or b) with at least two of the probes specifically hybridizing to a target sequence or its complement, comprising codon 90.~~

6. **(Twice Amended)** Method according to claim 1 further characterized in that:

step b) comprises amplifying a fragment of the protease gene with at least one 3'-primer specifically hybridizing to a target sequence located at nucleotide position 253 (codon 85) to position 300, in combination with at least one suitable 5'-primer~~, and~~

~~step c) comprises hybridizing the polynucleic acids of step a) or b) with at least two of the probes specifically hybridizing to a target sequence or its complement, comprising any of codons 30, 46, 48, 50, 52, 54, 82 and 84.~~

7. Method according to claim 5, further characterized in that the 5'-primer is SEQ ID NO: 5 and the 3'- primer is one primer or a combination of primers chosen from the following primers: SEQ ID NO: 4, SEQ ID NO: 506, SEQ ID NO: 507, SEQ ID NO: 508 and SEQ ID NO: 509.

8. Method according to claim 6, further characterized in that the 5'-primer is one primer or a combination of primers chosen from the following primers: SEQ ID NO: 3, SEQ ID NO: 503, SEQ ID NO: 504 and the 3'-primer is SEQ ID NO: 6.

~~9. (Amended) A probe as defined in claim 1 for use in a method for determining the susceptibility to antiviral drugs of HIV viruses in a biological sample, comprising SEQ ID NO: 267.~~

12. **(Twice Amended)** A diagnostic kit enabling a method for determining the susceptibility to antiviral drugs of HIV viruses in a biological sample, with said kit comprising:

a) when appropriate, a means for releasing, isolating or concentrating the polynucleic acids present in said sample;

b) when appropriate, at least one of the primers comprising SEQ ID NO: 3, SEQ ID NO: 503, SEQ ID NO: 504, SEQ ID NO: 4, SEQ ID NO: 506, SEQ ID NO: 507, SEQ ID NO: 508 or SEQ ID NO: 509; or

a 5'-primer specifically hybridizing to a target sequence located at nucleotide position 210 to 260 of the protease gene; or

a 3'-primer specifically hybridizing to a target sequence located at nucleotide position 253 (codon 85) to 300 of the protease gene;

c) at least two probes that specifically and simultaneously hybridize to a target sequence of HIV protease gene, ~~said target sequence selected from the group consisting of codon 30, codon 46 and/or 48, codon 50, codon 54, codon 82 and/or 84, codon 90~~ **codon 82/84,** fixed to a solid support, wherein said probes are capable of simultaneously hybridizing to their respective targets under appropriate hybridization and wash conditions;

d) a hybridization buffer, or components necessary for producing said buffer;

e) a wash solution, or components necessary for producing said solution;

f) when appropriate, a means for detecting the hybrids resulting from the preceding hybridization;

g) when appropriate, a means for attaching said probe to a solid support.

13. **(Amended)** The method according to claim 1, wherein at least two probes are provided for hybridizing to each of the target sequences of codon 30; codon **46/48** ~~46 and/or 48~~; codon 50; codon 54; codon **82/84** ~~82 and/or 84; or~~ **and** codon 90.

14. The method according to claim 13, wherein said probes are between 10 and 25 nucleotides in length and have a Tm between 36°C and 44°C.

15. The method according to claim 13, wherein said probes are capable of hybridizing to their respective target sequences under stringent hybridization conditions carried out at 39°C.

16. The method according to claim 15, wherein said probes are selected from the group consisting of SEQ ID NO: 7 to SEQ ID NO: 477, SEQ ID NO: 510 to SEQ ID NO: 519 and the complements thereof.

17. (Amended) The kit according to claim 12, wherein at least two probes are provided for hybridizing to each of the target sequences of codon 30; codon ~~46 and/or 48~~ **46/48** codon 50; codon 54; codon ~~82 and/or 84; or~~ **82/84 and** codon 90.

18. The kit according to claim 17, wherein said probes are between 10 and 25 nucleotides in length and have a Tm between 36°C and 44°C.

19. The kit according to claim 17, wherein said probes are selected from the group consisting of SEQ ID NO: 7 to SEQ ID NO: 477, SEQ ID NO: 510 to SEQ ID NO: 519 and the complements thereof.

20. **(Amended)** A solid support for use in the method of claim 1, said support having two or more probes immobilized thereon, wherein said probes are capable of specifically and simultaneously hybridizing to a target sequence of the HIV protease gene, **codon 82/84 or** ~~said target sequence selected from the group consisting of codon 30, codon 46 and/or 48, codon 50, codon 54, codon 82 and/or 84, codon 90 and~~ the complement thereof.

21. **(Amended)** The solid support of claim ~~20~~ **25** wherein the probes are selected from the group consisting of SEQ ID NOs. 7-477.

~~22. The solid support of claim 20 wherein at least two probes are specific for codon 82.~~

23. **(Amended)** The solid support of claim ~~22~~ **20** wherein the probes are selected from the group consisting of SEQ ID. NOs. 228-357.

24. **(Amended)** The solid support of claim ~~22~~ **20** comprising SEQ ID NO. 267 and SEQ ID NO. 354.

25. **(Amended)** The solid support of claim 20 comprising at least two probes for each target sequence of codon 30, codon ~~46 and/or 48~~ **46/48**, codon 50, codon 54, codon ~~82 and/or 84~~ **82/84**, and codon 90.

26. **(Amended)** A composition comprising at least two probes fixed to a solid support for use in the method of claim 1, wherein said probes are capable of specifically and simultaneously hybridizing to a target sequence of the HIV protease gene, **codon 82/84 or** ~~said target sequence selected from the group consisting of codon 30, codon 46 and/or 48, codon 50, codon 54, codon 82 and/or 84, codon 90 and~~ the complement thereof.

27. The composition of claim 26, wherein the probes are further provided with a poly-T-tail.

28. **(New)** The method according to claim 1, further comprising hybridizing at least two probes to an additional target sequence selected from the group consisting of codon 30; codon 46/48; codon 50; codon 54; and codon 90.

29. **(New)** The method according to claim 28, wherein said probes are selected from the group consisting of SEQ ID NO: 7 to SEQ ID NO: 477, SEQ ID NO: 510 to SEQ ID NO: 519 and the complements thereof.

30. **(New)** The method according to claim 1, wherein said probes are SEQ ID NO: 267 and SEQ ID NO: 354.

31. **(New)** The method according to claim 1, wherein the target sequences for codon 82/84 are shown in Figure 1.

32. **(New)** The method according to claim 13, wherein the target sequences for each codon are shown in Figure 1.

33. **(New)** The method according to claim 28, wherein the target sequences for each codon are shown in Figure 1.